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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,170	KAWAOKA, YOSHIHIRO	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-35* is/are pending in the application.

4a) Of the above claim(s) *12-14 and 16-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Request for Continued Examination

1) A request for continued examination under 37 C.F.R 1.114, including the fee set forth in 37 C.F.R 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R 1.114, and the fee set forth in 37 C.F.R 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R 1.114. Applicant's submission filed on 10/18/04 has been entered.

Applicant's Amendment

2) Acknowledgment is made of Applicant's amendment filed 09/17/04 in response to the final Office Action mailed 07/13/04. With this, Applicant has amended the specification.

Status of Claims

3) Claims 1, 33 and 35 have been amended via the amendment filed 09/17/04.

Claims 1-14 and 16-35 are pending.

Claims 1-11 and 32-35 are under examination.

Prior Citation of Title 35 Sections

4) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

5) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

6) The rejection of claims 1-4 and 8 made in paragraph 13 of the Office Action mailed 01/15/04 and maintained in paragraph 13 of the Office Action mailed 07/13/04 under 35 U.S.C. § 102(b) as being anticipated by Martin *et al.* (*Virology* 241: 101-111, 1998) or Brandli *et al.* (*J. Biol. Chem.* 263: 16283-16290, 1988), is withdrawn in light of the modified rejection made below.

7) The rejection of claim 33 and those dependent therefrom made in paragraph 15 of the Office Action mailed 07/13/04 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn upon further consideration.

8) The rejection of claim 33 made in paragraph 16(a) of the Office Action mailed 07/13/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's

amendment to the claim.

9) The rejection of claim 35 made in paragraph 16(b) of the Office Action mailed 07/13/04 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

Rejection(s) Maintained

10) The rejection of claim 1 made in paragraph 11 of the Office Action mailed 01/15/04 and maintained in paragraph 12 of the Office Action mailed 07/13/04 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is maintained for reasons set forth therein and herebelow. Dependent claims 8-11 and 32-35 are now added to this rejection.

Applicant cites case law and contends that the words 'vertebrate' and 'mammalian' readily convey distinguishing information concerning identity such that one of ordinary skill in the art could visualize or recognize the identity of the members of the genus. Applicant points to claims 2 and 7 and submit that the specification describes the use of two lectins known to bind to sialic acid containing molecules for mammalian cells and avian cells. Applicant states that Table 4 in Chapter 51 of Fields *Virology*, 1985 lists cells from organisms recognized as being susceptible to influenza virus infection. Applicant concludes that he/she has conveyed identifying characteristics of the genus of claimed mutant cells by disclosing a functional characteristic coupled with a known or disclosed correlation between function and structure.

Applicant's arguments have been carefully considered, but are non-persuasive. The independent claim 1 does not recite the words 'vertebrate' or 'mammalian' cells. Claim 1 broadly recites a 'mutant cell', which encompasses non-vertebrate mutant cells, non-mammalian mutant cells, eukaryotic mutant cells and prokaryotic mutant cells etc. However, such mutant cells having the recited characteristics, i.e., decreased levels of sialic acid-containing host cell receptors for influenza virus relative to a corresponding wild-type cell which wild-type cell supports efficient influenza virus replication, are not described either in the specification or in the Fields *Virology* such that one of skill in the art could identify the members of the genus. The rejection stands.

11) The rejection of claim 1 and those dependent therefrom made in paragraph 14 of the Office Action mailed 07/13/04 under 35 U.S.C. § 112, first paragraph, as containing new matter, is maintained for reasons set therein.

Applicant contends that the specification at lines 18-21 on page 1 of the specification

describes that the hemagglutinin (HA) of influenza virus binds sialyl oligosaccharides, oligosaccharides containing terminal sialic acid linked to galactose, on host cell surface glycoproteins. Applicant states that lines 21 and 22 of page 2 of the specification disclose that the mutant cell of the invention has altered expression of sialic acid containing host cell receptors. Applicant states that lines 15-28 of page 3 of the specification disclose that cells are contacted with agents that bind to sialic acid in the context of other linked molecules. Applicant therefore opines that the phrase 'sialic acid-containing molecule' is supported by the specification.

Applicant's arguments have been carefully considered, but are non-persuasive. The background of the invention at lines 18-21 of page 1 of the specification is not Applicant's invention. The recited 'sialic acid containing host receptors' (for which Applicant has support) are not the same as the 'sialic acid-containing molecules' in terms of scope. The original claim 12 has support for the limitation: 'lectin specifically binds sialic acid'. The terms 'sialic acid' and 'sialic acid-containing host cell receptors' do not provide support for the full scope of the term 'sialic acid-containing molecules'. The rejection stands.

Response to Applicant's Arguments on Martin *et al.* and Brandli *et al.*

12) Applicant acknowledges that Martin's MDCK RCA^r cells have a 70 to 75% reduction in cell surface sialic acid and that Brandli's mutant cells had 70 to 75% decreased binding to a lectin, which binds sialyl residues. However, Applicant states that MDCK RCA^r cells bound wheat germ agglutinin which is specific for *N*-acetylneuraminic acid and *N*-acetylglucosamine and argues that none of the cites references discloses a cell line which has reduced levels of terminal sialic acid, e.g., reduced levels of N-acetylneuraminic acid.

Applicant's arguments have been carefully considered, but are not persuasive. Claims 1-4 and 8 are product-by-process claims which require that the isolated mutant cell comprise decreased levels of 'sialic acid-containing host cell receptors for influenza virus' relative to a corresponding wild-type cell which wild-type cell supports efficient influenza virus replication. Claim 1 does not identify the lectin by its name. The prior art mutant MDCK RCA^r cells, having 70 to 75% reduction in cell surface sialic acid (i.e., neuraminic acid) compared to the wild-type cells, meet the claim limitations. The first line of claim 1 does not require the decreased levels of sialic acid present on the mutant cell to be 'terminal' sialic acid. Even if it did, that the reduced levels of sialic acid present on the prior art mutant cells are indeed terminal sialic acid (N-acetylneuraminic acid) is

inherent from the teachings of Martin *et al.* and Brandli *et al.* in light of what is well known in the art. For instance, it is well known in the art that the cell surface receptors that are recognized by influenza virus do contain terminal neuraminic (sialic) acids. See for example section 0054 of Doyle *et al.* US 20040132164. Martin *et al.* specifically taught that the 70-75% reduced levels of cell surface sialic acid receptors present on their isolated mutant MDCK RCA^r (Madin-Darby canine kidney) cells are specific for influenza virus. It was also known in the art at the time of the invention that the neuraminic acid to which influenza virus preferentially binds is *N*-acetyl neuraminic acid linked to galactose by alpha(2-3) or alpha(2-6)Gal-*N*-acetylgalactosamine, the former specific to *Sambucus nigra* lectin and the latter specific to *Maackia amurensis* lectin. For example, see abstract and pages 3357 and 3358 of Ito *et al.* (*J. Virol.* 71: 3357-3362, 1997). Ito *et al.* taught that MDCK cells contain both the linkages (see abstract). Therefore, Martin's or Brandli's MDCK RCA^r cells are expected to bind to a lectin such as *Sambucus nigra* lectin and *Maackia amurensis* lectin. See art rejections below.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

13) Claims 1-11 and 32-35 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 1 is vague and indefinite in the limitations: 'mutant cell comprising .... sialic acid-containing' (see lines 1 and 2) and 'mutant cell selected for ..... terminal sialic acid' (see last two lines). The earlier recited limitation 'sialic acid' is much broader in scope than the latter limitation 'terminal sialic acid' recited in the last two lines of the claim. It is unclear whether the claimed mutant cell has decreased levels of any sialic acid containing receptors, or decreased levels of terminal sialic acid containing receptors.

(b) Claims 34 and 35 are confusing and/or improperly broadening in scope in the limitation 'the lection specifically binds sialic acid', because claims 34 and 35 depend from claim 1, which as amended, includes the limitation 'a lectin which binds terminal sialic acid'. The limitation 'sialic acid' in claims 34 and 35 is much broader in scope than the limitation in the base claim, 'terminal sialic acid'.

(c) Claims 2-11 and 32-35, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

14) Claims 1-4, 8, 32, 34 and 35 are rejected under 35 U.S.C. § 102(b) as being anticipated by Martin *et al.* (*Virology* 241: 101-111, 1998, already of record) or Brandli *et al.* (*J. Biol. Chem.* 263: 16283-16290, 1988, already of record) as evidenced by Doyle *et al.* (US 20040132164) and Ito *et al.* (*J. Virol.* 71: 3357-3362, 1997).

It is noted that claim 1 is a product claim that includes the process limitation: 'wherein the mutant cell is selected for .....'. It is further noted that the 'sialic acid-' recited in line 1 of claim 1 is not required to be 'terminal sialic acid'.

Martin *et al.* taught isolated mutant MDCK RCA^r (Madin-Darby canine kidney) cells that have 70-75% reduced levels of cell surface sialic acid receptors specific for influenza virus. The mutant cells were susceptible to infection by influenza virus (see abstract; page 106; and Figures 4 and 5).

Brandli *et al.* taught isolated mutant MDCK (Madin-Darby canine kidney) cells that have 70-75% reduction in sialic acid receptors (see abstract; Experimental Procedures; Results; and pages 16286 and 16287).

The limitations 'wherein the mutant cell is selected for ..... molecules' in claim 1 represent process limitations. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicant has not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicant has not shown the underlying structure of the prior art mutant MDCK cell differs from that of the instantly claimed mutant cell.

That the prior art mutant cells contain reduced levels of terminal sialic acid, i.e., terminal N-acetylneuraminic acid, is inherent from the teachings of Martin *et al.* or Brandli *et al.* in light of what is well known in the art. For instance, it is well known in the art that the cell surface receptors

that are recognized by influenza virus do contain terminal neuraminic (sialic) acids (see section 0054 of Doyle *et al.*). Martin specifically taught that the 70-75% reduced levels of cell surface sialic acid receptors present on the isolated mutant MDCK RCA^r (Madin-Darby canine kidney) cells are specific for influenza virus. It was also known in the art at the time of the invention that the neuraminic acid to which influenza virus preferentially binds is *N*-acetyl neuraminic acid linked to galactose by alpha(2-3) or alpha(2-6)Gal-*N*-acetylgalactosamine, the former specific to *Sambucus nigra* lectin and the latter specific to *Maackia amurensis* lectin. For example, see abstract and pages 3357 and 3358 of Ito *et al.* (*J. Virol.* 71: 3357-3362, 1997) which also taught that MDCK cells contain both the linkages (see abstract). Therefore, Martin's or Brandli's MDCK RCA^r cells are expected to bind to a lectin such as *Sambucus nigra* lectin and *Maackia amurensis* lectin.

The disclosure of Martin *et al.* or Brandli *et al.* anticipates the instant invention. The reference of Doyle *et al.* or Ito *et al.* is **not** used as a secondary reference in combination with Martin *et al.* or Brnadli *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Martin *et al.* or Brandli *et al.*, because Doyle *et al.* or Ito *et al.* teach the recited inherent properties of the mutant cell. See *In re Samour* 197 USPQ 1 (CCPA 1978).

Claims 1-4 and 8 are anticipated by Martin *et al.* or Brandli *et al.*

15) Claims 1, 8, 32, 34 and 35 are rejected under 35 U.S.C. § 102(b) as being anticipated by Matta *et al.* (*Parasitol Res.* 85: 293-299, 1999).

It is noted that the 'cell' recited in claim 1 encompasses any cell including a non-mammalian and non-vertebrate cell.

Matta *et al.* taught an isolated TFR^{R1} mutant cell population of *C. fasciculata* which showed a low level of reactivity with *Sambucus nigra* lectin (sialic acid alpha 2-3Gal-specific) and *Maakia amurensis* lectin (sialic acid alpha 2-6Gal-specific) compared to the wild type cells (see last paragraph under 'Results' and page 296, right column) and therefore contained decreased levels of sialic acid. It is taught that influenza virus recognizes cell-surface glycoconjugates containing terminal sialic acid (neuraminic acid) residues (see paragraph bridging pages 293 and 294).

The limitations 'wherein the mutant cell is selected for ..... molecules' in claim 1 represent process limitations. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicant has not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicant has not shown the underlying structure of the prior art mutant MDCK cell differs from that of the instantly claimed mutant cell.

Claims 1, 8, 32, 34 and 35 are anticipated by Matta *et al.*

Remarks

16) Claims 1-11 and 32-35 stand rejected.

17) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300.

18) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

19) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

December, 2004

S. DEVI, PH.D.
PRIMARY EXAMINER